

## Prevalence of Ocular *Demodex* Infestation among Cataract Surgery Cases

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### Abstract

**Purpose:** *Demodex* infestation is associated with increased ocular surface inflammation. In patients undergoing cataract surgery, high counts of *Demodex* mites may increase the risk of perioperative complications. The objective was to evaluate the prevalence of *Demodex* infestation, as well as, host related factors and surgical complications in cataract surgery candidates.

**Methods:** 150 cataract patients, scheduled for surgery, were evaluated for *Demodex spp.* 4 to 8 eyelashes were obtained by depilation and they were observed under an optical microscope to quantify the number of mites present. The prevalence was calculated and an adjustment was made using logistic regression models with the SAS V9.4 program.

**Results:** *Demodex* prevalence was 67.6% (95%CI 63.7 - 75.2), which is significantly higher to prior reports among elderly Hispanics (50 years or older,  $p < 0.0001$ ) and one report in similarly aged individuals ( $p < 0.0001$ ). Moreover, it was age-dependent ranging from 5.9% in 40-50 up to 32.7% in 70 - 80 years old. Surgical complication rates were not significantly different between exposed and unexposed cases.

**Conclusion:** Demodicosis prevalence among the elderly is significantly higher among those evaluated and undergoing cataract surgery. Despite not finding postoperative complications due to the exhaustive control in surgical practice, it is important to search for *Demodex* prior to surgery to prevent postoperative complications.

**Keywords:** *Demodex*; Ocular Infestation; Blepharitis; Prevalence; Cross-Sectional Study; Cataract Surgery

### Introduction

*Demodex* is a common ectoparasite in the human skin associated with several conditions in the anterior segment of the eye [1]. The species found in the eyelashes (*D. folliculorum*), the pilosebaceous, and meibomian glands (*D. brevis*) are plausible causative agents of blepharitis, keratitis, conjunctivitis, and meibomian gland dysfunction among other inflammatory eye diseases [2-7]. Several mechanisms might explain *Demodex*'s role in these pathologies, including hosting bacterias that induce hypersensitivity reactions, claws-related microabrasions leading to hyperkeratinization and hyperplasia, and mechanical obstruction of the sebaceous glands [3,8].

The prevalence of ocular demodicosis is age-dependent, affecting up to 84% of the population aged 60 [3]. In older adults, additional factors such as a higher sebaceous secretion and broadening of the follicular opening contribute to the pathogenesis and proliferation of

the mites [9]. Even though the proportion of affected individuals varies significantly across reports, middle-aged and elderly adults are at greater risk for symptomatic infection and complications [10].

Cataracts are also a common cause of consultation among this population. Starting at the age of 40, the risk of developing lens opacifications increases with each decade of life [11]. To date, the average age of cataract surgery is 67.7 years [12]. Thus, *Demodex* infestation may be a common condition among cataract surgery candidates. In addition, *Demodex*-induced ocular inflammation may increase perioperative complications [13].

### Objective of the Study

The objective was to evaluate the prevalence of *Demodex* infestation, as well as host related factors and surgical complications in cataract surgery candidates.

### Methods

We performed a cross-sectional study of 150 age-related cataract cases undergoing surgery. We included patients aged 18 years or older, who agreed to participate after informed consent, and no history of systemic antiparasitic, antibiotic treatments, or topical eye antibiotics in the past six months. We excluded those cases with seborrheic blepharitis, those who received any drug treatment, or used any eyelid cleansing solution. For each eligible case, we abstracted clinically meaningful data from electronic medical records, conducted a thorough standard ophthalmic exam, and assess for any surgical complications (Posterior capsule tear/rupture; Cystoid macular edema; Choroidal detachment; Descemet membrane detachment) at 24-hours or one-week postoperatively. For each patient, we took a sample of two eyelashes per eyelid (eight per patient) and placed the sample in slides with 100ml of physiologic saline solution covered with a coverslip for light microscopy at 40X and 100X (zeiss axio imager z2 microscope). Additionally, the infestation index was estimated by taking the ratio of the absolute count of *Demodex* for each sampled eyelash [14-16]. This study followed the tenets of the Helsinki Declaration of Human Studies and has been approved by the ethics committee of our institution.

### Statistical analysis

Numerical data were reported as the mean values and standard deviations for continuous data and relative frequencies for categorical data. We used the independent samples t-test to continuous variables and Chi-square tests to categorical variables. All these statistical analyses were performed using the software SAS v.9.4. [17].  $P < 0.05$  considered significant. The estimation of the unadjusted and adjusted *Demodex* spp prevalence, with a 95% confidence interval, was in Rv.3.5.1 using the EpiR package [18]. To bolster our approach, additionally ran a series of probit logistic regression models to adjust *Demodex* spp prevalence for clinically meaningful variables (e.g. age, sex, ocular comorbidities) and those with marginal significance in univariate analysis (BMI).

### Results

A detailed description of our sample is shown in table 1. The age means of population studied was 68 years ( $\pm 12.3$  years), and men and women were equally distributed. The crude prevalence of *Demodex* spp was 67.3%, and there was a 20% probability of infestation and at least one *Demodex* per eyelash (Table 1). Most importantly, the surgical complication rates at 24-hours or one-week postoperatively were not significantly different between exposed and unexposed cases to *Demodex* (Table 2). In relation to other comorbidities; one-third of our population had diabetes or hypertension, and most did not have any other ocular comorbidities (Table 1).

Characteristic	N (%)*
<i>Demodex spp</i>	101 (67.3)
<i>Demodex spp</i> (Count), mean $\pm$ SD	1.5 $\pm$ 1.5
Index of infestation, mean $\pm$ SD	0.2 $\pm$ 0.2
<b>Sociodemographics</b>	
Age (years), mean $\pm$ SD	68.1 $\pm$ 12.3
< 30	1 (0.7)
30 - 40	1 (0.7)
40 - 50	8 (5.3)
50 - 60	32 (21.3)
60 - 70	31 (20.7)
70 - 80	47 (31.3)
80 - 90	29 (19.3)
> 90	1 (0.7)
<b>Sex</b>	
Males	68 (45.3)
Females	82 (54.7)
BMI (kg/m <sup>2</sup> ), mean $\pm$ SD	27.2 $\pm$ 4.5
<b>WHO categories</b>	
<18.5	1 (0.7)
[18.5 - 25)	44 (29.3)
[25 - 30)	73 (48.7)
[30 - 35)	24 (16.0)
[35 - 40)	6 (4.0)
$\geq$ 40	2 (1.3)
<b>Systemic comorbidities</b>	
Type 2 Diabetes	54 (36.0)
Hypertension	50 (33.3)
<b>Ocular comorbidities</b>	
None (other than cataract)	135 (90.0)
Age-related macular degeneration	3 (2.0)
Glaucoma	7 (4.7)
Diabetic retinopathy	2 (1.3)
<b>Surgical techniques and outcomes</b>	
Phacoemulsification + Intraocular lens	142 (94.7)
Extracapsular cataract extraction	8 (5.3)
Any surgical complication <sup>^</sup>	12 (8.0)
Posterior capsule tear/rupture	9 (6.0)
Cystoid macular edema	1 (0.7)
Choroidal detachment	1 (0.7)
Descemet membrane detachment	1 (0.7)

**Table 1:** Description of the sample (n = 150).

\*: Numbers may not sum to totals due to missing data, and column percentages may not sum to 100% due to rounding.

<sup>^</sup>: Any surgical complication at 24-hours or one-week postoperatively.

BMI: Body Mass Index.

[Caption] Full sample description. Means and standard deviations, along with sample size and column percentages are shown.

**Bivariate and adjusted *Demodex* spp prevalence**

To identify if any clinical characteristics or demographics were significantly associated with demodicosis, we performed bivariate analysis (Table 2). By this method, there was a marginally significant association between BMI and demodicosis status (yes vs. no). On average, *Demodex* infested cases were on average 1.5 years younger ( $p = 0.0541$ ). However, when stratifying by BMI categories (WHO) there was no significant difference in categories proportions (Table 2).

Characteristic	<i>Demodex</i> spp		p
	Yes (N = 101)	No (N = 49)	
<b>Sociodemographics</b>			
Age (years), mean ± SD	68.6 ± 12.0	67.0 ± 13.1	0.4659
< 30	0 (0.0)	1 (2.0)	0.4073
30 - 40	1 (1.0)	0 (0.0)	
40 - 50	6 (5.9)	2 (4.1)	
50 - 60	21 (20.8)	11 (22.5)	
60 - 70	18 (17.8)	13 (26.5)	
70 - 80	33 (32.7)	14 (28.6)	
80 - 90	22 (21.8)	7 (14.3)	
> 90	0 (0.0)	1 (2.0)	
<b>Sex</b>			
Males	44 (43.6)	24 (49.0)	0.5321
Females	57 (56.4)	25 (51.0)	
BMI (kg/m <sup>2</sup> ), mean ± SD	26.7 ± 4.0	28.2 ± 5.1	0.0541
<b>WHO categories</b>			
< 18.5	0 (0.0)	1 (2.0)	0.1072
[18.5 - 25)	34 (33.7)	10 (20.4)	
[25 - 30)	49 (48.5)	24 (49.0)	
[30 - 35)	14 (13.9)	10 (20.4)	
[35 - 40)	4 (4.0)	2 (4.1)	
≥ 40	0 (0.0)	2 (4.1)	
<b>Systemic comorbidities</b>			
Type 2 Diabetes	36 (35.7)	18 (36.7)	0.8961
Hypertension	34 (33.7)	16 (32.7)	0.9020
<b>Ocular comorbidities</b>			
None (other than cataract)	88 (87.1)	47 (95.9)	0.4676
Age-related macular degeneration	4 (4.0)	0 (0.0)	
Glaucoma	4 (4.0)	3 (6.1)	0.6833
<b>Diabetic retinopathy</b>			
<b>Surgical techniques and outcomes</b>			
Phacoemulsification + Intraocular lens	96 (95.1)	46 (93.9)	0.7165
Extracapsular cataract extraction	5 (5.0)	3 (6.1)	
Any surgical complication <sup>^</sup>	9 (8.9)	3 (6.1)	0.5232
Posterior capsule tear/rupture	6 (5.9)	3 (6.1)	
Cystoid macular edema	1 (1.0)	0 (0.0)	
Choroidal detachment	1 (1.0)	0 (0.0)	
Descemet membrane detachment	1 (1.0)	0 (0.0)	

**Table 2:** Description of the sample by *Demodex* spp status (n = 150).

\*: Numbers may not sum to totals due to missing data, and column percentages may not sum to 100% due to rounding.

<sup>^</sup>: Any surgical complication at 24-hours or one-week postoperatively.

BMI: Body Mass Index.

[Caption] Stratified characteristics by case/control status. Marginally significant differences are italicized and were computed with Student's t-Test (Continuous variables) or  $\chi^2$  test (categorical variable).

To provide a more accurate demodicosis prevalence among our studied population, we adjusted our estimations for several clinical parameters by probit logistic regression (Table 3). Our most parsimonious and significant model indicates that age-related cataract cases undergoing surgery have a *Demodex spp* prevalence of 67.60% (95%CI 63.74, 75.15). This finding is significantly higher from one prior report in similarly aged Hispanics (44.0% vs. 93.1%,  $p < 0.0001$ ) (Table 4). However, among the elderly (> 60) we have a higher age specific *Demodex spp* prevalence compared to other populations (Figure 1).

<b><i>Demodex spp</i> prevalence</b>	<b>P% (95% CI)</b>
Crude	67.33 (59.21, 74.80)
Adjusted for age, sex, BMI	67.40 (63.52, 75.00)
Adjusted for † and DM, HTN, any ocular comorbidities	63.67 (56.79, 77.15)
Most parsimonious adjustment (only BMI)	67.60 (63.74, 75.15)

**Table 3:** Crude and covariate-adjusted *Demodex spp* prevalence among cataract patients undergoing a surgical procedure.

†: Age, sex, and BMI covariates.

BMI: Body Mass Index.

[Caption] Statistical adjustment of demodicosis prevalence by a probit logistic regression taking several clinical and demographic covariates.

<b>Author, Year</b>	<b>Demodicosis prevalence</b>	<b>p-value *</b>
Davalos, 2020	<ul style="list-style-type: none"> <li>• Estimated prevalence among cataract cases undergoing surgery: 67.6%</li> <li>• Prevalence among ≥ 50 years of age: 93.1%</li> <li>• Prevalence among ≥ 65 years of age: 62.4%</li> <li>• Prevalence among 50-60 years of age: 20.8%</li> <li>• Prevalence among 50-65 years of age: 30.7%</li> <li>• Prevalence among 60-70 years of age: 17.8%</li> <li>• Prevalence among 70-80 years of age: 32.7%</li> </ul>	Ref.
Biernat, 2018 [20]	<ul style="list-style-type: none"> <li>• Prevalence among 51-65 years of age: 25.0%</li> </ul> → Prevalence among 50-65 years of age: 30.7% <ul style="list-style-type: none"> <li>• Prevalence among ≥ 65 years of age: 33.3%</li> </ul> → Prevalence among ≥ 65 years of age: 62.4% <p>Studied population from Poland.</p>	0.1881  < 0.0001
Velasco and Levy, 2017 [21]	<ul style="list-style-type: none"> <li>• Pooled prevalence in cases ≥ 50 years of age: 44.0%</li> </ul> → Prevalence among ≥ 50 years of age: 93.1% <p>Studied Hispanics from Guadalajara, Mexico.</p>	< 0.0001
Wesolowska, 2014 [6]	<ul style="list-style-type: none"> <li>• Prevalence among 60-70 years of age: 73.3%</li> </ul> → Prevalence among 60-70 years of age: 17.8% <ul style="list-style-type: none"> <li>• Prevalence among 70-80 years of age: 75.0%</li> </ul> → Prevalence among 70-80 years of age: 32.7% <p>Studied population from Poland.</p>	< 0.0001  < 0.0001

**Table 4:** Comparison between the covariate-adjusted *Demodex spp* prevalence among cataract patients undergoing a surgical procedure and elderly demodicosis prevalence.

\* P-value from a goodness of fit  $\chi^2$  test evaluated with one degree of freedom.

– Reference study.

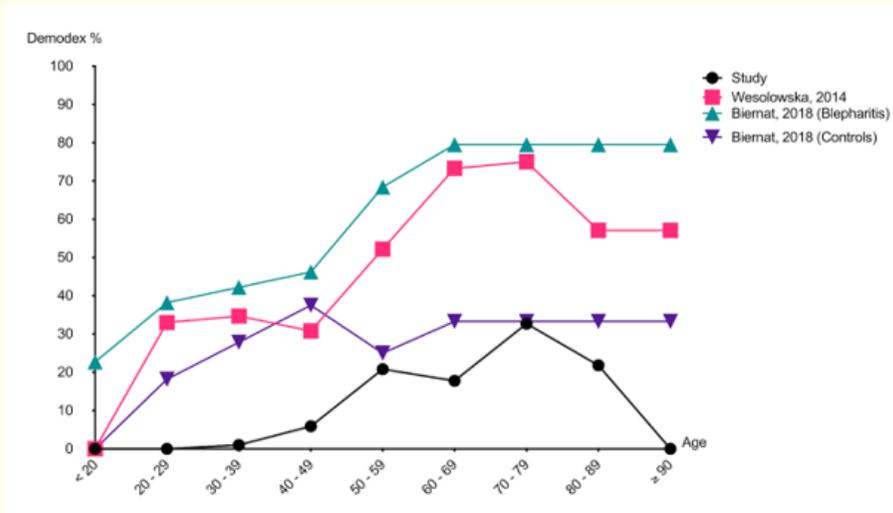


Figure 1: Overview of the microbiota-gut-brain axis and its bidirectional crosstalk.

Finally, to tease the effect modification of BMI on demodicosis prevalence, we stratified our covariate-adjusted *Demodex spp* prevalence by BMI categories (Figure 2). Interestingly, there is an inverse relationship between BMI and *Demodex* proportion. However, this finding is marginally significant and should be taken cautiously.

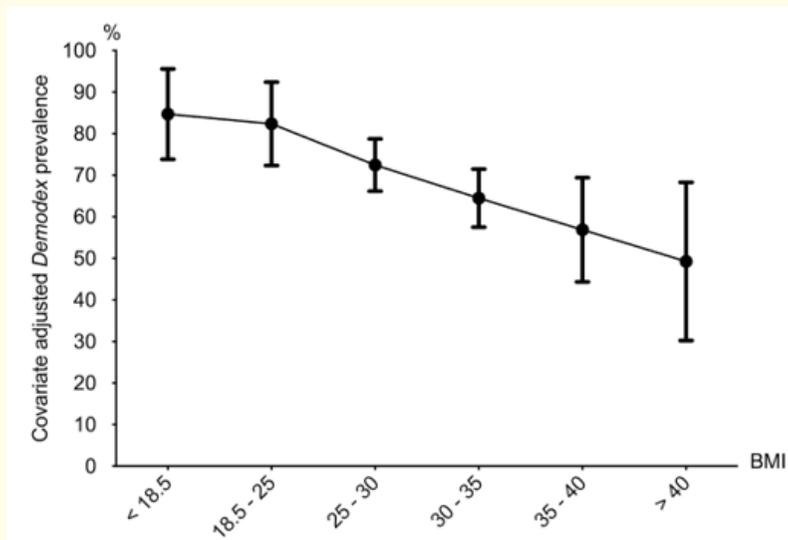


Figure 2: Covariate-adjusted *Demodex spp* prevalence by body-mass index categories.

## Discussion

The demodicosis prevalence estimated among cases undergoing cataract surgery was 67%. In a previous report, with a similarly aged population, was reported 33% patients with demodicosis, our results were significantly higher. In another study with elderly Hispanics,

the prevalence reported was 44%. These results suggest that in patients from the Mexican population there could be a greater presence of *Demodex* and this would increase the risk of postoperative complications, however, more studies are needed to verify the finding [2-7].

In our population, *Demodex* status had no association with surgical complications within 24-hours and one week after the procedure. These findings suggest that asymptomatic *Demodex* infestation is unlikely to affect anterior segment intraocular surgery outcomes.

The prevalence of *Demodex* infestation is highly aged-dependent. Similarly, to previous reports, our findings showed that adults aged 50 and over are more prone to ocular demodicosis. Interestingly, we observed an increased prevalence of infestation in cases undergoing cataract surgery compared with similar age groups. *D. folliculorum* inhabits the skin of the cheeks, nose, temples, eyebrows and other regions of the face, *D. brevis* is more commonly localized in the neck and chest, we hypothesize that facial and eye manipulation during pre-surgical evaluation might partially explain the high proportion of *Demodex* positive cases [2,9,19]. Because postoperative long-term outcomes of *Demodex* infestation are still unclear, we suggest clinicians take the appropriate sanitary measurement and limit facial contact, especially when assessing elderly patients.

Moreover, our findings showed that *Demodex* infestation has an inverse correlation with BMI within our population. It is plausible that socioeconomic, individual factors and comorbidities contribute to mites proliferation in asymptomatic cases.

### Conclusions

The surgical complications cannot be attributed to a pathogen, since these are common adverse outcomes of the procedure itself.

Asymptomatic ocular demodicosis is a highly comorbid condition in cataract surgery candidates. *Demodex* status is not associated with an increased proportion of adverse outcomes during the short-term postoperative period.

However, despite not finding postoperative complications due to the exhaustive control in surgical practice, it is important to search for *Demodex* prior to surgery to prevent postoperative complications.

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### Conflicts of Interest

None of the authors have any proprietary interests or conflicts of interest related to this submission.

This manuscript has not been published anywhere previously and it is not simultaneously being considered for any other publication.

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